WEST Search History

DATE: Thursday, December 04, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=JPAB,EPAB,DWPI; PLUR=NO; OP=ADJ			
L26	L25 and @pd<20000307	8	L26
L25	L23 and (tumor$3 or tumour$3 or cancer$3 or malignan$3 or neoplas$3)	17	L25
L24	L23 and (mammary or breast or mamma)	3	L24
L23	NIS or hNIS or ((sodium near (iodine or iodide)) near3 (transporter or symporter or channel))	806	L23
DB=USPT; PLUR=NO; OP=ADJ			
L22	L21 or l20	10	L22
L21	L19 near3 (antibod$3 or immunoglobulin$1)	8	L21
L20	anti adj2 L19	4	L20
L19	Ct1 or Ct2 or (Ct adj (1 or 2))	2980	L19
DB=PGPB; PLUR=NO; OP=ADJ			
L18	l16 near3 (antibod$3 or immunoglobulin$1)	1	L18
L17	anti adj2 L16	0	L17
L16	Ct1 or Ct2 or (Ct adj (1 0r 2))	706	L16
L15	L13 and @prad<20000307	0	L15
L14	L13 and @ad<20000307	0	L14
L13	L12 same l11	6	L13
L12	(breast or mammary or mamma)	15946	L12
L11	L10 or l9	333	L11
L10	NIS	324	L10
L9	(sodium near (iodine or iodide)) near3 (transporter or symporter or channel)	18	L9
DB=USPT; PLUR=NO; OP=ADJ			
L8	l7 and (breast or mammary or mamma)	3	L8
L7	l3[ti,ab]	19	L7
L6	L5 and l3	2	L6
L5	(breast or mammary or mamma)[ti,ab]	2788	L5
L4	L3 same (breast or mammary or mamma)	2	L4
L3	L2 or l1	1186	L3
L2	NIS	1178	L2
L1	(sodium near (iodine or iodide)) near3 (transporter or symporter or channel)	12	L1

END OF SEARCH HISTORY

WEST

Generate Collection Print

L13: Entry 1 of 6 File: PGPB Aug 7, 2003

DOCUMENT-IDENTIFIER: US 20030147881 A1
TITLE: Method for preparation of single chain antibodies

Detail Description Paragraph (233):
[0256] 1.3 Na.sup.+/I.sup.- Symporter (NIS) Both rat and human NIS, a membrane-bound glycoprotein which is responsible for the thyroid gland's ability to concentrate iodide up to 40-fold with respect to plasma, was recently cloned,.sup.117,118 and its genomic structure analyzed..sup.119 hNIS has 643 amino acid and a proposed secondary structure containing 13 transmembrane helices. NIS was upregulated with trans-retinoic acid in breast cancer cell line MCF7..sup.120 Prostate cell lines transfected with hNIS linked to a PSA promoter became sensitive to radioiodine therapy..sup.121,122 Adenovirus-mediated.sup.123 or retrovirus-mediated.sup.124 transfer of rat NIS into human carcinoma lines and human glioma cell lines.sup.125 enabled rapid perchlorate-sensitive radioiodine uptake, in some cases to >200 fold. Xenografted tumors injected intratumorally with this adenovirus became iodine-avid accumulating 11% ID/gm. Prostate cancer (LNCaP) transfected ex vivo with the hNIS retained 25-30% of the total radioiodine with a biologic half-life of 45 h (30-60 h) and produced tumor shrinkage..sup.122 The slow efflux of iodide from NIS transduced cells can be partly explained by their lack of the efflux pump pendrin,.sup.126,127 found exclusively in the thyroid but not other normal tissues.

Detail Description Paragraph (235):
[0258] Neither NK92 nor CIR-gene modified T-cells expressed SSTR2 or showed spontaneous uptake of .sup.111In-Octreotide; thus SSTR2 gene transduction is necessary for imaging purposes. Surface receptor SSTR2 versus enzyme HSV1-tk approach have recently been compared in vitro and in vivo. Although uptake was equally good in vitro, in vivo imaging with HSV1-tk appeared inferior to SSTR2..sup.96 We expect radiometal labeled peptides to be rapidly endocytosed following binding to SSTR2, and become trapped intracellularly, unlike radioiodine which is metabolized and released. One major disadvantage of SSTR2 is its presence in a large spectrum of neuroendocrine tumors; here T-cell trafficking and tumors may not be easily distinguishable. Nevertheless, most sarcomas.sup.128 and high risk (in contrast to low risk) neuroblastoma.sup.129 have low expression of SSTR2. HNIS has a clear advantage over SSTR2 since few tumors except thyroid and possibly breast cancers express this protein. Although NIS can be transfected into human cells to express functional protein, the cellular consequences of the ectopic ion channel or iodine accrual on the human lymphocytes are unknown. There is also the concern on the membrane trafficking of the symporter. Although the leader sequence in the pVector would enhance membrane localization of the transgene, the rate of symporter turnover could affect the amount of radioiodine uptake. The efflux of iodide and consequently the short cellular half life can also be a limitation, especially if repeated imaging studies are needed. Nevertheless, this is a surmountable issue since radioactive iodine can always be readministered. Ironically this efflux could be an advantage, since radioactive iodide is rapidly excreted and less likely to damage lymphocyte function. It is conceivable that if retention of the iodide is needed, NK92 line can first be transfected with thyroid peroxidase enzyme to ensure organification..sup.130 One unique advantage of HSV1-tk is its suicide function that kills transduced cells in the presence of ganciclovir. Nevertheless, hNIS-transduced lymphocytes can potentially be killed by high dose of .sup.131I or .sup.124I, as demonstrated in NIS-gene modified tumor cell lines.sup.120,122-125 and the thyroid gland.

Detail Description Paragraph (423):
[0445] 120. Kogai T, Schultz J J, Johnson L S, et al: Retinoic acid induces sodium/iodide symporter gene expression and radioiodide uptake in the MCF-7 breast cancer cell line. PNAS (USA) 97:8519-8524, 2000

```
     (FILE 'HOME' ENTERED AT 16:54:28 ON 04 DEC 2003)

     FILE 'REGISTRY' ENTERED AT 16:54:56 ON 04 DEC 2003
L1             0 S MGNIS
L2             0 S NEDLLFFLGQKELE/SQSP
L3             7 S KELEGAGSWTPCVGHD/SQSP
L4             8 S GHDGGRDQQETNL/SQSP
L5             0 S NEDLLFFLGQKELE/SQSP

     FILE 'CAPLUS' ENTERED AT 17:00:40 ON 04 DEC 2003
L6             5 S L3
L7             6 S L4
L8             0 S L6 AND ((BREAST OR MAMMARY OR MAMMA#)(5A)(TUMOR? OR TUMOUR? O
L9             0 S L7 AND ((BREAST OR MAMMARY OR MAMMA#)(5A)(TUMOR? OR TUMOUR? O
L10            0 S L6 AND ADENOCARCINOMA#
L11            0 S L7 AND ADENOCARCINOMA#

     FILE 'DGENE' ENTERED AT 17:02:50 ON 04 DEC 2003
                RUN GETSEQ
                ---------
L12   RUN STATEMENT CREATED
                RUN GETSEQ
                ---------
L13   RUN STATEMENT CREATED
                RUN GETSEQ
                ---------
L14   RUN STATEMENT CREATED

     FILE 'PCTGEN' ENTERED AT 17:10:32 ON 04 DEC 2003
                RUN GETSEQ
                ---------
L15   RUN STATEMENT CREATED
                RUN GETSEQ
                ---------
L16   RUN STATEMENT CREATED

     FILE 'MEDLINE, BIOSIS, SCISEARCH, CANCERLIT, LIFESCI, BIOTECHDS, CAPLUS'
     ENTERED AT 17:28:52 ON 04 DEC 2003
L17          419 S ((SODIUM OR NA#)(A)(IODINE OR IODIDE OR I#))(3A)(COTRANSPORTE
L18       633428 S (BREAST# OR MAMMAR? OR MAMMA#)(3A)(TUMOR? OR TUMOUR? OR CANCE
L19            4 S L17 AND L18

     FILE 'PCTFULL, USPATFULL, EUROPATFULL' ENTERED AT 17:34:51 ON 04 DEC 2003
L20           63 S (SODIUM)(A)(IODINE OR IODIDE)(3A)(TRANSPORTER OR COTRANSPORTE
L21         4640 S (NA(A)I)
L22           39 S L21(3A)(TRANSPORTER OR COTRANSPORTER OR SYMPORTER OR CHANNEL#
L23           92 S L20 OR L22
L24        53939 S (BREAST OR MAMMAR? OR MAMMA#)(5A)(TUMOR? OR TUMOUR? OR CANCER
L25           12 S L23(S)L24
L26            1 S L22/TI,AB
L27           10 S L23/TI,AB
L28            5 S L27 AND L24

     FILE 'CAPLUS' ENTERED AT 17:58:13 ON 04 DEC 2003

     FILE 'PCTFULL, USPATFULL, EUROPATFULL' ENTERED AT 18:00:57 ON 04 DEC 2003
L29          453 S (SODIUM OR IODINE)(3A)(TRASNPORTER OR COTRANSPORTER OR SYMPOR
L30           21 S L29(S)L24
L31         8142 S CT1 OR CT2 OR (CT(W)(1 OR 2))
L32          240 S ANTI(2W)L31
L33          216 S L31(3A)ANTIBOD?
L34          270 S L32 OR L33
L35          122 S L34(S)L24
```

```
L36          120 S L34(5A)L24
L37        51869 S (BREAST OR MAMMAR? OR MAMMA#)(3A)(TUMOR? OR TUMOUR? OR CANCER
L38          118 S L37(S)L34
L39            7 S L38 AND PD<20000307

=> s l34/ti,ab
L40            0 L34/TI,AB
```